Single Lung Transplant vs Double Lung Transplant: A Single-Center Experience With Particular Consideration for Idiopathic Pulmonary Arterial Hypertension

Remigiusz Antończyk[a,b], Tomasz Stącel[a], Maciej Urlik[a], Magdalena Latos[a,b,*], Michał Kręt[a], Dawid Borowik[a], Marta Wajda-Pokrontka[a,b], Fryderyk Zawadzki[a,b], Zofia Tatoj[a,b], Piotr Przybyłowski[a,c], Marian Zembala[a,b], Marek Ochman[a,b], and Mirosław Nęcki[a]

[a]Silesian Center for Heart Diseases, Zabrze, Poland; [b]Department of Cardiac, Vascular, and Endovascular Surgery and Transplantology, Medical University of Silesia, Katowice, Poland; and [c]First Chair of General Surgery, Jagiellonian University, Medical College, Kraków, Poland

ABSTRACT

Background. Lung transplant remains the only viable treatment for certain patients with end-stage lung diseases. Such patients can become either single or double lung recipients. The 2 procedures are associated with specific risks and benefits. The aim of the study was to assess the survival of patients after lung transplant in a single center.

Methods. The retrospective study consists of 128 lung transplant recipients. Patients underwent transplant between 2004 and 2017 because of following diseases: chronic obstructive pulmonary disease (28.2%), cystic fibrosis (26.5%), and primary pulmonary hypertension (12.3%), including idiopathic pulmonary arterial hypertension and interstitial lung diseases (33%). Patients with idiopathic pulmonary arterial hypertension were not treated with postoperative extracorporeal membrane oxygenation as left heart conditioning.

Results. Regardless of underlying disease, 75% of DLT recipients and 51% of SLT recipients reached 5-year survival ($P = .0066$). A total of 87% of lung transplant recipients with cystic fibrosis reached 1-year survival. Among lung recipients with primary pulmonary hypertension who underwent DLT and SLT, 5-year survival was reached by 84% and 51%, respectively ($P = .025$). Among patients with chronic obstructive pulmonary disease, 82% of DLT recipients and 62% of SLT recipients reached 1-year survival ($P = .22$). Patients who received transplants because of primary pulmonary hypertension presented the worst short-term survival among all SLT recipients.

Conclusions. Patients with CF have the best overall survival among all lung transplant recipients. Double lung transplant provides statistically significantly better outcomes than single lung transplant. This observation is also present among recipients who underwent transplant because of primary pulmonary hypertension, as single lung transplant is not recommended among such patients in particular.

LUNG transplant is the only available treatment for certain types of end-stage lung disease. Although single lung transplants (SLTs) were the performed more often during the time this therapeutic option first gained recognition as a way of treatment, most present-day procedures are double lung transplants (DLTs) [1]. There are some contraindications for performing SLT. Patients with cystic fibrosis are eligible only to become double lung recipients because of the characteristics of their disease. On the other hand, patients with pulmonary fibrosis and

*Address correspondence to Magdalena Latos, MD, Medical University of Silesia, Silesian Centre for Heart Diseases, ul. Marii Skłodowskiej-Curie 9 Pawilon C, 41-800 Zabrze, Poland. Tel: +48667288893. E-mail: latos.magdalena93@gmail.com

0041-1345/20
https://doi.org/10.1016/j.transproceed.2020.03.046

chronic obstructive pulmonary disease (COPD) can become a single lung recipient [2–4]. Available literature reports various conclusions whether patients with those diseases benefit more from either of these procedures [4,5]. Some studies emphasize that in the scarcity of organs for transplant, performing 2 SLTs can save 2 potential candidates [4]. Despite that, DLT is more beneficial for more urgent candidates with high lung allocation score [6]. Superior long-term survival is more often observed after DLT [1,7]. Single lung procedures are discouraged among patients with mean pulmonary artery pressure exceeding 30 mm Hg [8]. DLT is also reported to provide good outcomes for patients with primary pulmonary hypertension [9]. The aim of the study was to assess the survival among double and single lung recipients from a single center.

METHODS

This retrospective study consisted of 128 lung transplant recipients who received transplants between 2004 and 2017 in a single center. Detailed characteristics pertaining to demographic and clinical features of the studied group is presented in Table 1. Retransplants and heart-lung transplants were excluded from the study. Patients, who underwent SLT were statistically significantly older than those after DLT. They also presented greater body mass index and forced expiratory volume in 1 second at qualification. SLT as a surgical procedure lasted shorter than DLT. Analysis assessed survival by means of Kaplan-Meier estimators performed for the entire

Table 1. Demographic and Clinical Data of Patients Who Underwent Either SLT (n = 38) or DLT (n = 90)

Variables	DLT	SLT	*P* Value
Recipient age, median (IQR), y	35 (23.5)	50 (16.3)	< .001
Recipient BMI, median (IQR)	19.6 (4.86)	21.93 (6.53)	< .001
Recipient pulmonary function at qualification			
FEV_1, median (IQR), %	24 (13.2)	30 (32.82)	< .001
FVC, median (IQR), %	40 (25.2)	45 (26)	.404
6MWD, median (IQR), mile	302.7 (153.12)	275.19 (141.96)	.296
Donor age, mean (SD), y	40.51 (11.93)	37.78 (13.62)	.264
Donor BMI, mean (SD)	23.64 (2.91)	22.76 (2.6)	.109
Donor hemoglobin, mean (SD), g%	11.01 (2.47)	11.18 (2.6)	.738
Donor serum creatinine, median (IQR), mg%	1.02 (0.75)	1.02 (0.73)	.751
Duration of operation, median (IQR), h	12.83 (2.5)	9.15 (2.84)	< .001
Ventilation time, median (IQR), h	24 (9.25)	17 (11.75)	.004
Total ischemia time, mean (SD), min	733.51 (397.12)	536.91 (248.61)	.009
Recipient sex, No. (%)			.455
Female	41 (45.56)	15 (39.47)	
Male	49 (54.44)	23 (60.53)	
Donor sex, No. (%)			.369
Female	36 (40)	12 (31.58)	
Male	54 (60)	26 (68.42)	
Blood type matching, No. (%)			.038
Compatible	18 (21.43)	15 (39.47)	
Identical	66 (78.57)	23 (60.53)	
Blood type, No. (%)			.208
O	40 (44.44)	16 (42.11)	
A	28 (31.11)	18 (47.37)	
AB	5 (5.56)	1 (2.63)	
B	17 (18.89)	3 (7.89)	
Underlying disease, No. (%)			.123
Chronic obstructive pulmonary disease	14 (15.56)	13 (34.19)	
Cystic fibrosis	44 (48.89)	1(5.26)	
Interstitial lung disease	10 (11.11)	8 (21.04)	
Idiopathic pulmonary arterial hypertension	8 (8.89)	8 (21.04)	
Combined pulmonary fibrosis and emphysema	1 (1.11)	0 (0)	
Bronchiolitis obliterans syndrome	1 (1.11)	0 (0)	
Emphysema	4 (4.44)	3 (7.89)	
Bronchiectasis	2 (2.22)	1 (2.63)	
Pneumoconiosis	2 (2.22)	0 (0)	
Hypersensitivity pneumonitis	2 (2.22)	2 (5.26)	
Langerhans cell histiocytosis	1 (1.11)	2 (5.26)	
Hereditary hemorrhagic telangiectasia	1 (1.11)	0 (0)	

Abbreviations: 6MWD, 6-minute walk distance; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IQR, interquartile range.

population as well as separately for DLT and SLT recipients who underwent transplant because of COPD, interstitial lung disease (ILD), and idiopathic pulmonary arterial hypertension (IPAH). Patients with cystic fibrosis were included in a study of the general population. However, there is no purpose in analyzing their survival depending on type of procedure because there is only 1 single lung recipient in the entire group. The classic threshold $\alpha = .05$ was considered the level of significance.

RESULTS

First analysis pertained to whether there is a difference among survival depending on the type of the procedure regardless of the underlying disease. Kaplan-Meier estimation resulted in assessing that survival after DLT was statistically significantly better than that obtained after SLT ($P < .05$). Detailed results are presented in Fig 1.

The same analysis was performed among patients who became graft recipients because of COPD. Among this group, results were not statistically significant ($P = .22$) nor were they among patients who received transplants because of ILD ($P = .66$). Survival analysis of those patients also determined that there is no statistically significant difference among recipients of either SLT or DLT ($P = .62$).

Final analysis was performed among patients who became either single lung recipients or double lung recipients because of IPAH. There was a statistically significant difference in survival in favor of DLT recipients among this group ($P = .0266$). Detailed results are demonstrated in Fig 2. Additional statistical analysis was performed to evaluate the potential differences in characteristics of the patients who underwent either DLT or SLT because of end-stage IPAH. No statistically significant differences were found among factors such as age of the recipient (Table 2). Patients who received transplants because of IPAH underwent operation with cardiopulmonary support present only intraoperatively. Extracorporeal membrane oxygenation was not used as a postoperative left heart conditioning tool.

DISCUSSION

Our study assessed that regardless of underlying disease, DLT provides a greater survival benefit than single lung procedure. This finding is consistent with the reports presented by the International Society of Heart and Lung Transplantation [1]. They report that median survival after DLT is 3 years longer than after SLT. What is more, the difference between conditional survival is almost 4.5 years in favor of DLT. Another statistically significant finding was that there is no advantage in performing SLT among patients with pulmonary hypertension, which is supported by studies published by Villavicencio et al and Nasir et al [8,10]. Those studies discourage transplant facilities from considering SLT among patients with pulmonary hypertension. Our data consist of patients who received transplants since 2004 up until 2017. During this time, none of the patients underwent left heart conditioning with the support of postoperative extracorporeal membrane oxygenation. Our analysis should discourage other

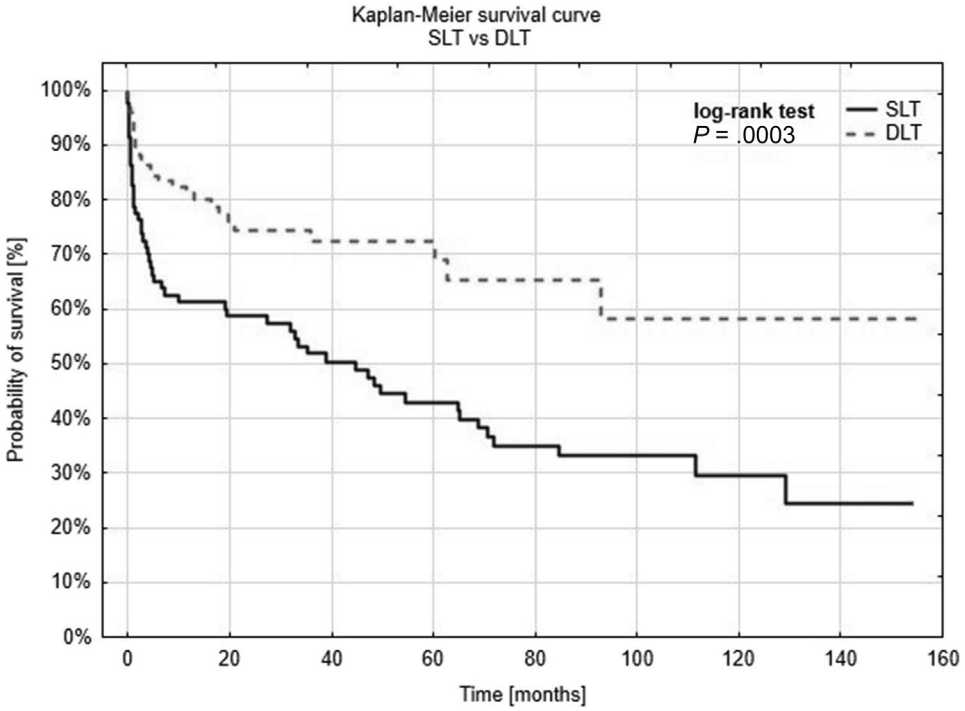

Fig 1. Kaplan-Meier estimation of survival among patients who underwent either DLT or SLT regardless of underlying disease. DLT, double lung transplant; SLT, single lung transplant.

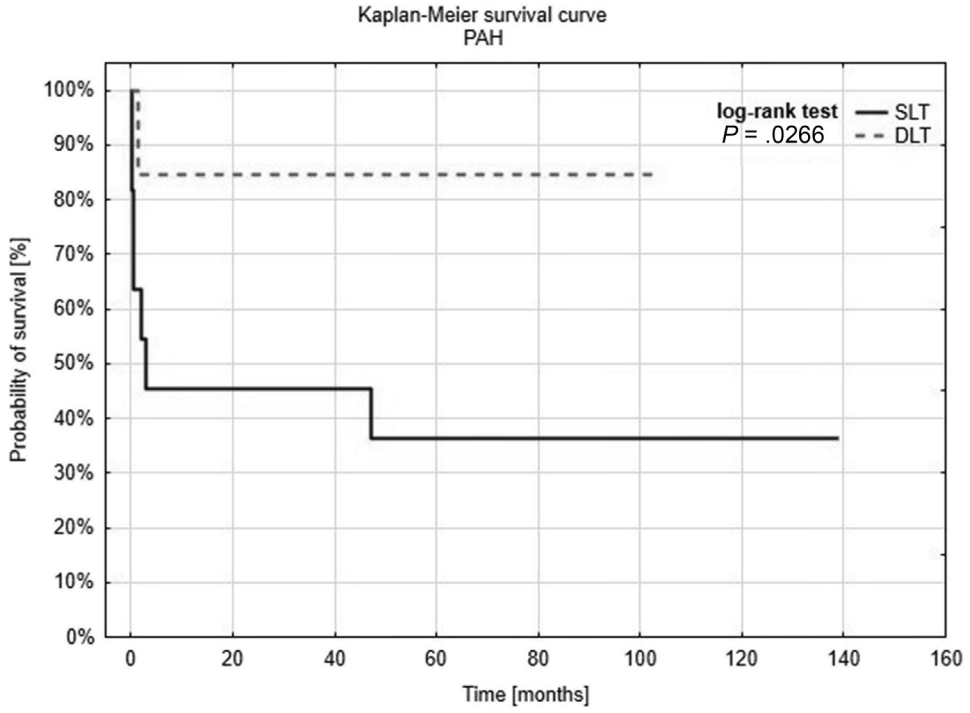

Fig 2. Kaplan-Meier estimation of survival among patients who underwent either DLT or SLT among patients with idiopathic form of PAH. DLT, double lung transplant; PAH, pulmonary arterial hypertension; SLT, single lung transplant.

transplant facilities from performing SLT for patients with end-stage IPAH as well as other patients with severe pulmonary hypertension. As also reported by the International Society for Heart and Lung Transplantation Registry, patients with IPAH present the worst short-term survival after lung transplant among all underlying diseases [1]. Our analysis did not prove that DLT is better therapeutic option for patients with COPD than SLT. Similar findings

Table 2. Demographic and Clinical Features at Qualification of Patients Undergoing Either SLT or DLT Because of Idiopathic Pulmonary Arterial Hypertension

Recipient Features at Qualification	SLT	DLT	*P* Value
Age at qualification (M±SD), y	33.63 ± 12.28	37.40 ± 8.53	.453
Age at transplant (M±SD), y	34.63 ± 12.77	37.70 ± 8.54	.549
BMI (M±SD), kg/m^2	20.18 ± 2.60	22.56 ± 3.32	.116
Serum creatinine (Me ± IQR), mg/dL	1.01 ± 0.26	1.05 ± 0.19	.759
INR (Me±IQR)	1.85 ± 0.51	1.79 ± 1.08	.902
Hematocrit (Me±IQR), %	41.51 ± 4.99	43.16 ± 3.03	.397
Hemoglobin (M±SD), g/dL	11.29 ± 3.00	13.21 ± 3.28	.218
NT-proBNP (Me±IQR), pg/mL	2043.23 ± 993.49	2144.68 ± 1547.41	.895
6MWD (M±SD), meters	394.50 ± 75.41	354.00 ± 115.03	.458
Oxygen saturation before 6MWT (M±SD), %	94.00 ± 6.48	94.50 ± 2.95	.841
Oxygen saturation before 6MWT (M±SD), %	86.25 ± 6.90	84.70 ± 10.60	.794
EF (LVEF) (Me±IQR), %	59.17 ± 5.85	65.67 ± 15.58	.351
RVSP (Me±IQR), mm Hg	90.50 ± 23.77	80.17 ± 18.81	.423
TAPSE (Me±IQR), mm	16.83 ± 2.93	15.33 ± 3.20	.375
MPAP (Me±IQR), mm Hg	57.29 ± 18.87	61.09 ± 12.69	.625
PCWP mean (Me±IQR), mm Hg	13.00 ± 4.04	10.88 ± 1.96	.208
CI (Me±IQR), L/min/m^2	2.10 ± 0.52	2.53 ± 0.55	.156
CO (Me±IQR), L/min	3.64 ± 1.02	4.56 ± 1.07	.113

Abbreviations: 6MWD, 6 minute walk test diatance; 6MWT – 6 minute walk test; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, cardiac index; CO, cardiac output; DLT, double lung transplantation; INR, international normalized ratio; IQR- interquartile range; LVEF, left ventricle ejection fraction; M, mean; Me, median; MPAP, mean pulmonary artery pressure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PCWP, pulmonary capillary wedge pressure; RVSP, right ventricle pulmonary pressure; SD, standard deviation; SLT, single lung transplantation; TAPSE, tricuspid annular plane systolic excursion.

pertaining to not only COPD but also pulmonary fibrosis was presented by Aryal and Nathan [2]. Their work concluded that lacking good-quality evidence makes it is difficult to make strong recommendations. No statistically significant difference was noted at 5-year survival among DLT and SLT recipients who received transplants because of COPD according to Schaffer et al [5]. On the other hand, Crawford et al assessed that DLT is associated with significant survival benefit in the assessment of 5-year mortality [7]. Our study also did not acquire statistically significant difference of survival among patients who received transplants because of pulmonary fibrosis. Our research showed no difference in survival among DLT and SLT recipients because of ILD and particularly because of idiopathic pulmonary fibrosis (IPF). There are studies consistent with these findings. Chauhan et al presented the study that concluded in stating there is no statistical difference in actuarial graft survival between recipients undergoing DLT vs SLT because of IPF [4]. Such conclusion is also present in an article published by Ranganath et al [3]. On the other hand, studies by Schaffer et al and Villavicencio et al argue that DLT is the superior method of lung transplant for every kind of pulmonary fibrosis and IPF alone. The International Society of Heart and Lung Transplantation presented the data of more than 18,000 lung transplant recipients with COPD. It was statistically significant that DLT provides better survival [1]. Similar results are reported regarding the diseases associated with pulmonary fibrosis. Study of almost 3000 patients with ILD but not idiopathic interstitial pneumonia and more than 14,000 patients with idiopathic interstitial pneumonia undeniably proves that DLT recipients have better survival [1].

CONCLUSIONS

Regardless of the underlying disease, DLT provides better survival outcomes than SLT. The same observation was also proved true for patients who underwent lung transplant because of IPAH. It is advised not to perform SLT when DLT is a viable option, especially for patients with severe pulmonary hypertension.

REFERENCES

[1] Chambers DC, Cherikh WS, Goldfarb SB, Hayes D Jr, Kucheryavaya AY, Toll AE, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult lung and heart-lung transplant report-2018; focus theme: multiorgan transplantation. J Heart Lung Transplant 2018;37:1169–83.

[2] Aryal S, Nathan SD. Single vs bilateral lung transplantation: when and why. Curr Opin Organ Transplant 2018;23:316–23. https://doi.org/10.1097/MOT.0000000000000527.

[3] Ranganath NK, Malas J, Phillips KG, Lesko MB, Smith DE, Angel LF, et al. Single and double lung transplantation have equivalent survival for idiopathic pulmonary fibrosis. Ann Thorac Surg 2020;109:211–7. https://doi.org/10.1016/j.athoracsur.2019.06.090.

[4] Chauhan D, Karanam AB, Merlo A, Tom Bozzay PA, Zucker MJ, Seethamraju H, et al. Post-transplant survival in idiopathic pulmonary fibrosis patients concurrently listed for single and double lung transplantation. J Heart Lung Transplant 2016;35:657–60. https://doi.org/10.1016/j.healun.2015.12.030.

[5] Schaffer JM, Singh SK, Reitz BA, Zamanian RT, Mallidi HR. Single- vs double-lung transplantation in patients with chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis since the implementation of lung allocation based on medical need. JAMA 2015;313:936–48. https://doi.org/10.1001/jama.2015.1175.

[6] Black MC, Trivedi J, Schumer EM, Bousamra M, van Berkel V. Double lung transplants have significantly improved survival compared with single lung transplants in high lung allocation score patients. Ann Thorac Surg 2014;98:1737–41. https://doi.org/10.1016/j.athoracsur.2014.05.072.

[7] Crawford TC, Lui C, Magruder JT, Ha JS, Higgins RS, Merlo CA, et al. Five-year mortality hazard is reduced in chronic obstructive pulmonary disease patients receiving double- vs single-lung transplants. J Surg Res 2019;237:118–25. https://doi.org/10.1016/j.jss.2018.04.048.

[8] Villavicencio MA, Axtell AL, Osho A, Astor T, Roy N, Melnitchouk S, et al. Single- versus double-lung transplantation in pulmonary fibrosis: impact of age and pulmonary hypertension. Ann Thorac Surg 2018;106:856–63. https://doi.org/10.1016/j.athoracsur.2018.04.060.

[9] de Perrot M, Granton JT, McRae K, Pierre AF, Singer LG, Waddell TK, et al. Outcome of patients with pulmonary arterial hypertension referred for lung transplantation: a 14-year single-center experience. J Thorac Cardiovasc Surg 2012;143:910–8. https://doi.org/10.1016/j.jtcvs2011.08.055.

[10] Nasir BS, Mulvihill MS, Barac YD, Bishawi M, Cox ML, Megna DJ. Single lung transplantation in patients with severe secondary pulmonary hypertension. J Heart Lung Transplant 2019;38:939–48. https://doi.org/10.1016/j.healun.2019.06.014.